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Welcome to Yale Cancer Answers with doctors Howard Hochster, Anees Chagpar and Steven Gore. I am Bruce Barber. Yale Cancer Answers is our way of providing you with the most up-to-date information on cancer care by welcoming oncologists and specialists, who are on the forefront of the battle to fight cancer. This week in honor of ovarian cancer awareness month, Dr. Hochster is joined by Dr. Elena Ratner and Mary Jane Minkin. Dr. Ratner is an Associate Professor of Obstetrics, Gynecology and Reproductive Sciences and Dr. Minkin is a Clinical Professor of Obstetrics, Gynecology and Reproductive Sciences at Yale School of Medicine. Dr. Hochster is a Professor of Medicine in Medical Oncology and Associate Director for Clinical Sciences at Yale Cancer Hospital.

Hochster Tell us a little bit about your area of expertise, it sounds like pretty long title, obstetrics, gynecology, reproductive science, blah, blah, blah, you know?

Ratner So my area of expertise is gynecologic cancers, so cancers of the ovary, of the uterus, of the cervix, and the vulva and so forth and Mary Jane and myself, particularly are interested in survivorship in those women, in particularly with menopause and sexuality.

Hochster I see and so, well tell us a little bit, it is ovarian cancer awareness month, so can you tell us a little bit about maybe some of the other GYN cancers, but particularly ovarian cancer and what people need to know for ovarian cancer awareness.

Ratner Sure. So ovarian cancer is known as the cancer that whispers. The reasons known is that it is because unfortunately these cancers continue to be diagnosed later in their stages. Women with ovarian cancer frequently do not have symptoms until cancers are more advanced, but we now know that that is not particularly true, that ovarian cancer might not be cancers that whisper, it might be that they are actually speaking and nobody is listening. There has been some recent literature that says the women with ovarian cancer even at early stages did have symptoms; symptoms like bowel symptoms, bladder symptoms, but it is very important to remember that those symptoms are also very normal in this kind of age population. So what separated women who subsequently developed ovarian cancer from those that just had normal hormonal symptoms, is that the women who had ovarian cancer had these symptoms every single day for 2 weeks versus women who just had a normal perimenopause or menopausal symptoms, those symptoms come and go.

Hochster So bowel cramps, bladder cramps, pelvic or lower abdominal discomfort, but if it happens everyday for 2 weeks, then people should be more concerned.

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Ratner Exactly, I mean at the end of the day, most likely it is not ovarian cancer. Ovarian cancer overall is not very common, only 1.5% of women ever develop ovarian cancer, but it is important to know because we are best advocates, so you have to pay attention to body and these symptoms are normal, they come and go, that is fine, but if they do not come and go, they just come and stay, then you just need to see a physician.

Hochster And then, what will the physician if they go to their gynecologist that they see regularly, what would then happen?

Ratner Yeah, so their provider usually would just take the history and listen to the symptoms, do pelvic exam and lot of these questions will be answered just by normal physical examination and they will frequently do ultrasounds. So there usually is a very straightforward way of working these things up.

Hochster And that is all office testing?

Ratner Correct.

Hochster Okay, that is a key thing to be aware of if these kind of symptoms persist, see your gynecologist and they can be diagnosed fairly routinely and so, what is it then about ovarian cancer in terms of presentation, in terms of spread and whatever can you tell us a little bit more about that?

Ratner Sure. So just like I mentioned before, you know, we continue to struggle with diagnosing these cancers early and that again comes both you know, we would need women to pay attention to their bodies and we ourselves need to do better with listening and working these things up. So, so much of what we do now is actually prevention. You know, in the older days, we concentrated on treatments for cancer, then we talked about cure for cancer, then we talked about early detection, and now the future is prevention and prevention really can only happen if we identify the women who are at higher risks for those cancers. We now believe that the great majority of these cancers as many cancers are somehow genetically related, so for example something called the BRCA gene, the gene that became widely known with Angelina Jolie and her article in New York Times, which is one of the genes that predisposes women to developing these cancers.

Hochster But she had breast cancer?

Ratner I don't think she had any cancer.

Minkin She didn't, but she had a family history of ovarian cancer. Hochster I see, but more commonly women have breast cancer with BRCA.

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Ratner Yep, so women with BRCA1 and BRCA2 gene are at risk for breast cancer and ovarian cancer as well as some other cancers.

Minkin One thing that I just like to recommend for the general public as a general OB/GYN is that in many situations birth control pills have started getting a bad rep – ‘Oh, I don’t like hormones’ - things like that, but just for general listeners that actually taking a birth control pill on a regular basis reduces your risk of getting ovarian cancer by about 50%, which is probably the most effective chemopreventive method we have out there. So if a young woman is trying to evaluate birth control methods for herself, just as a general rule, if she is a good candidate for birth control pills that is an excellent method of chemoprevention for her in the long run.

Hochster Good to know. I’m glad you brought that up.

Ratner That is exactly what Mary Jane is talking about. You know, so much of what we do now is prevention. You know, first identifying women who are at risk to genetic testing, you know we will be listening to the family history, trying to pick out whether somebody truly has cancer that runs in the families and secondly as Mary Jane said, prevention. Birth control pills are fantastic, you know somebody who takes them for 5 years decreases their risk by 50%. Somebody who takes it for 10-15 years can decrease it for as high as 90%, it is incredible reduction. Hochster And we used to think that the BRCA only ran in families who are – where it’s clear that people had in every generation, young people had it, but now the American College of Obstetrics and Gynecology recommends that every woman who has ovarian cancer be tested, it is much more common than we thought, is that correct.

Ratner That is exactly correct. You know, we used to think that this is only limited to women of Ashkenazi Jewish ethnicity. We know now that is not the case. There are many other ethnicities that also have higher risk of these BRCA mutation and yes, every single woman with BRCA mutation with ovarian cancer now has to be tested for BRCA mutation, not just for family but also for the treatments because that really changes her treatment as well.

Hochster And the family history can be helpful if you have a very big family, but with smaller families today, sometimes they aren’t so predictive.

Ratner Exactly. That is exactly correct. We actually see a lot of women who get diagnosed with BRCA mutation just because they wanted to because their families were so small.

Minkin And one thing to remember is that the father side of the family is important too, we have mom and we have a dad, and then indeed the BRCA mutations can be passed on through the dad. So you want to know your father’s family history as well as your mom’s.

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Hochster Right, right, very true. Ok. So other familial kind of syndromes in ovarian cancer other than BRCA that people should be aware of?

Ratner There is some that are more popular, there is some that are less, that is why we are such strong supporters of genetic counselors who are specific professionals who would take your family history and make a big pedigree and really see if you are at risk for any familial genetic disorders, but there is something called Lynch syndrome, which predisposes women to colon cancer, uterine cancer, and ovarian cancer.

Hochster Right, uterine cancer is the second most common for Lynch symptoms.

Ratner That is right, and ovarian is third so 15% of women with Lynch syndrome can develop ovarian cancer. So yes, so there is definitely familial symptoms out there that should be aware of if you feel that the cancers is running in your family because that would be one of those things you can do, knowledge is power.

Hochster So while we are talking about uterine cancer, so if you go every year to a gynecologist, you go for the pelvic exam and they do a Pap smear. Does that help with detection of ovarian cancer?

Ratner It does not. Pap smears are only detection for cervical cancer and even though, it is not 100% perfect. But uterine cancer is a little bit easier than ovarian cancer. With uterine cancers, there is usually symptoms. Any woman who has gone through menopause and now has any sort of vaginal bleeding, that is abnormal. You know, I always tell providers that if a woman is diagnosed with uterine cancer at a later stage, that is our failure. We as providers need to tell all women that if you have any bleeding after menopause that is not normal and you need to see a provider, so that is why most women with uterine cancer actually get diagnosed at their earlier stage because they have symptoms, they see their physician, and they get diagnosed.

Hochster Again, the Pap smear does not detect ovarian cancer, where you need different kinds of detection, are blood tests helpful?

Ratner No, with uterine cancer, again it is truly just symptoms. If anybody has bleeding, they usually get again a physical examination, a biopsy, and an ultrasound and that is usually how it is.

Hochster Can ovarian, blood test for ovarian cancer.

Ratner Yes, but that is a more difficult question, yes, in women who are at higher risk for ovarian cancers, we do this screening where we do ultrasounds and a blood test called CA-125, it is a tumor marker, it is not a great test, we do not love CA-125, but it is kind of the best we got. So we use CA-125 in combination with ultrasounds knowing that a lot of time CA-125 can be either falsely positive or falsely negative, so it is not anything we would recommend routinely.

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Minkin Right and getting back to as you mentioned earlier ACOG recommendations. ACOG actually does not recommend doing routine blood tests, CA-125, or routine ultrasounds just as general screening, only looking for high risk folks and what happens to my patients periodically and I would say it happens once every year or two. They are blast emails that go out to the universe, I do not know where they come from, saying go talk to your doctor about getting CA-125 and I have a bunch of nervous folks coming in, we did not do a CA-125 and I said 'No, nor do you need one,' so as a routine screen, unfortunately it fails.

Hochster It is not sufficiently productive, so that it should be used for general screening, only people who are at high risk. And in terms of ovarian cancer awareness, any other symptoms that people get they should be aware off, that you know would be of concern to get to your doctor.

Ratner So ovarian cancers, usually happen after menopause or kind of around the time of menopause and that is a little bit of challenging. There is a lot of women who go through some changes during that time, so some weight gain, some bloating, some bowel symptoms, and that is all normal. I think it is very important to remember that ovarian cancer in general is not very common and most symptoms are just normal menopausal symptoms, but again the symptoms of bowel cramping, bladder symptoms, urinary tract infections that just keep coming, bloating, you know all of a sudden you feel like you need to get go shopping and get a bigger size of clothes, fatigue, stuff like that.

Hochster Some of that bloating can be actually accumulating fluid in the abdomen which is something to see the doctor about.

Minkin And there is one symptom because of course bloating, I would happens in 100% of menopause ladies. I do not see one person who is just not complaining about bloating and of course, people get panicky, you know, obviously I do lots of exams and lots of ultrasounds on folks. One symptom that may be helpful, not saying this has to be a demarcating symptom, but that if a woman complains in a fancy word as I explained to patients is early satiety, I feel full soon, I take 3 spoons of food and I am done, I don't feel like eating any more, that is something you got to pay attention to, you really do need to pay attention to that. So certainly is pay attention to bloating, but if you start feeling with feelings with early fullness, please call your medical care provider.

Hochster So bloating to the extent where you need to let out your pants, early satiety, pain, things that don't go away in a couple of weeks, they are there everyday, these are symptoms to be aware for ovarian cancer awareness, does not mean you got it, but it means go get checked out. Okay. We are going to take a short break for medical minute. Please stay tuned to learn more information about ovarian cancer with Dr. Elana Ratner and Dr. Mary Jane Minkin.

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Hochster Welcome back to Yale Cancer Answers. This is Dr. Howard Hochster and I am joined tonight by my guests, Dr. Elana Ratner and Dr. Mary Jane Minkin and we are discussing ovarian cancer. So we have been discussing some of the symptoms that people should be aware of for ovarian cancer that might lead to a physician visit and to be evaluated. So can you tell us a little bit about what happens if people have a suspected ovarian cancer, what is happening in diagnosis and then in treatment?

Ratner So the paradigm of treatment for ovarian cancer is drastically changing. We have treatments today that we did not have 3 months ago. We, in ovarian cancer, truly now believe in personalized therapy and targeted approach, so in the older days, like 2 years ago, everybody would just used to get the same chemotherapy and most women would respond, now a days that is not the case, nowadays here at Smilow, we test every single tumor, we know exactly what kind of mutations the tumor has and then the women gets personalized treatments, treatment specifically for her and for her tumor. So chemotherapies are easier, some of them are now oral, so women do not even have to come into my office to get them and the success is greater and the toxicity is less.

Hochster That is very very encouraging. So does surgery still play a role in the treatment of ovarian cancer?

Ratner That is old days, surgery is kind of the big part of treatment for ovarian cancer, the goal of the surgery is to remove all of the cancer and leaving nothing behind, those are the women that do really well and then once the tumor is all removed surgically, then we treat microscopic cells with treatment with chemotherapy or these targeted approaches.

Hochster And that is a normal thing, but sometimes you start with chemotherapy first in some cases.

Ratner Yeah, most of the time we do, but even in those cases, we always try to find something a little bit extra, something that would work a little bit better than the standard.

00:17:38 into MP3: https://ysmwebsites.azureedge.net/cancer/2017-YCA-0910-Podcast-Ratner_314872_5_v1.mp3 Hochster Okay and for the patients with BRCA mutations that we talked about, there is a new drug that has been approved, there is a little bit of different approach now?

Ratner Right, so that is one of the examples that I was referring to. The women with BRCA mutation, there is now a drug that we had been waiting for for a long time for that to become FDA approved, which it now is and it is a pill that works specifically for DNA repair, these cells have been unable to fix themselves, so all the cancer cells die and it is an oral drug, there is now 3 of them, that are all FDA approved and are oral, so women take them at home and do not even come into office.

Hochster And you use that instead of chemotherapy?

Ratner Very frequently, we use it instead of chemotherapy, but it is not just for women with BRCA mutation. Only 10% of women that we know have the BRCA mutation, but we now think that additional good probably 30% have a BRCA mutation in their tumors. So they themselves do not have it, so they cannot pass it on to the daughters or their sons, but the tumors has it and that is a great thing for us because it gives us the opportunity to be able to treat it with this pill.

Hochster So there are 2 things; one you test the tumor itself for any DNA abnormalities in mutations which are not necessarily inherited, mostly those are acquired because tumors go bad, but sometimes it is inherited like in the germline BRCA inherited syndrome, but sometimes the tumors have them, any way, these kinds of pills would work in either case?

Ratner Exactly, so very many times the women come and we get the blood testing done and they are so disappointed that they do not have the mutation, but that is actually not the most common way that we will treat these mutations, most of them will actually be in the tumor and not in the blood.

Hochster Then they don't have to worry about passing it on?

Ratner Exactly.

Hochster So that is really important.

Ratner It is kind of a double benefit. You know, that they do not pass it on to their children, but yet it gives us an opportunity to be able to target those mutations.

Hochster I see. So you two said in the beginning that you were interested in survivorship and what happens after treatment for ovarian cancer, can you tell us a little bit about what you are working on in that area?

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Ratner Yes, that is a big thing with Mary Jane, that is our passion. We really want to not just treat the women with ovarian cancer and uterine cancer and breast cancer, not just cure them, but we want to assure that they have a great quality of life during treatment and after treatment. We always have to remember that these women, normal young women, that just happened to be diagnosed with the disease and you know, they wake up one day and their life is different. You know, they are getting chemotherapy, things are not the same. So what we try to do is we instill that sense of normalcy, give them their lives back, you know, these women just want to get in the car and drive the kids to school and then go on a date with their husband and that is what we are trying to do. We want to kind of instill back the normalcy that they lost during the treatment.

Minkin Yeah and we started a program here about 10 years ago now for women. We started off with gynecologic cancer patients, but we can now extend it to, you know, cancer survivors to deal with issues of sexuality, intimacy, and menopause and we indeed call that our SIMS Clinic, sexuality, intimacy and menopause and we indeed call her at SIMS Clinic, sexuality, intimacy, and menopause for survivors and for example, a simple thing that women who have had ovarian cancer, many of them are indeed candidates for hormone replacement therapy, many women are not aware of that and that certainly enhances quality of life for many of these women and certainly, if these women are dealing with sexuality problems, things like vaginal dryness, and stuff after having surgery and chemotherapy, that we can address these with a lot of therapies, vaginal therapies, and other kinds of medications that can be very helpful and can restore a very normal sex life. The other thing that we do with our clinic - our SIMS Clinic, is we have strong support from the psychology department and every one of our patients meets with a member of our psychology team to talk about some of the really profound changes that can occur to emotional issues to psychological issues with sex and we can schedule ongoing therapy with the psychology team if some counseling is in order. So it really works out very nicely to try to join both the physical issues, hormonal issues, and psychological issues for many of our survivors who do need a little bit of help that way and we are hoping we are enhancing quality of life significantly.

Hochster I'm sure and so I want to emphasize while you started focusing on women with gynecologic cancers, this is common for women who have had any kind of cancer and you see them in your clinic if they are having these issues?

Minkin Absolutely, we see again a lot of breast cancer survivors, colon cancer survivors, who had radiation therapy and even we have a lot of people that we see, even hematological cancers present with some gynecologic manifestations believe it or not, so we see lots of different folks and we are just delighted to be able to help them.

Ratner We most recently were able expand this program to include not just women, but also men and there is now an extension of the program within the urologic department with Dr. Stan Honig who now also takes care of men and

the counseling that Mary Jane referred to with Dr. Dwain Fehon is also for couples, so that is one of the beauties of this program is that we do not just take care of the women, we are able to care of the couple, of the family, and so forth.

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Hochster And can you tell us a little bit more about some of the things that you do in the clinic then?

Minkin Oh sure, the other thing we should mention before getting into other things is we see a lot of young women who come in carrying the diagnosis of BRCA folks, who themselves have not yet fortunately been diagnosed with a tumor, but find out they are carriers and they are going to be having preventative surgery like having their ovaries removed, but many of these women are having their ovaries taken out at a very young age to prevent the cancer from occurring which is what we want to do, but again the good news is that many of these women, hormone therapy is quite reasonable and we like to start talking about it long before they have surgery, we talk about what is going to happen after surgery, how we are going to help you after surgery, and we have a lot of data out there showing that hormone therapy in these women is really quite safe and actually helpful for their long term health. So we are trying to start doing the counseling early before they actually have surgical interventions, but certainly as far as our interventions with a lot of these women, that we deal with hormonal medications, nonhormonal medications, we do a lot of work with dilator therapy for a lot of these women, particularly those who have had some radiation therapy, where we see a lot of folks to help them. So there are a lot of interventions that we can do to really make their lives much better.

Hochster And for the women who are the BRCA carriers, the education sounds like it is really really important, but there is also screening and so forth, do you do that in your clinic?

Ratner So we do that, we have a separate clinic where we take care of women with BRCA mutations or other mutations or women who are deemed to be at higher risk for ovarian cancer. Yes, we have high risk clinic that we really just deal with women who we believe to be at high risk. I just want again to emphasize the point that Mary Jane made just now - Mary Jane and I are going to be jumping over each other to tell you stuff. It is so imperative that women with BRCA mutation know that they are candidates for hormone replacement after their surgery. A lot of this women undergo these, we call them risk-reducing surgeries where the ovaries and fallopian tubes are removed as young as age 35. I see a lot of patients, a lot of young women, who are referred to me from the community that after these women have the surgery, they are not placed on hormones, because providers believe that because they have the BRCA mutation, it is not safe for them to be on hormones.

Hochster So just what happens is that after your ovaries are removed even at

a very young age, you become immediately menopausal, you don't have the female hormones that are normally made, so you are saying it is safe for them to get these hormones even though they have a BRCA syndrome.

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Minkin Yes, not only safe, but better for their quality of life and the other thing that I want to mention is as far as a quasi-prevention issue, but I really want to make an advertisement here, if the young woman is diagnosed with any kind of cancer, you know, hematological cancer, lymphomas, whatever, that one thing we would also to try to do is to get the word out to these young women and their oncologists that they should work on preservation of fertility for after their chemotherapy, it is a very important area and so if any of our listeners, you know, know somebody, who has gotten - unfortunately a young woman who has been diagnosed with a tumor, give us a call, we want to see you, because we can basically help these young women obtain eggs that can be frozen very nicely and be available after they are, you know, cured from their cancer, they have had their chemotherapy, which unfortunately can interrupt fertility for some of these young women earlier on in their lives, but we can actually save eggs, so if they want to become moms, they can become moms.

Hochster And that is a pretty routine thing even today?

Minkin It is and many people are not aware of it and many people of course panic the minute you hear the word cancer, understandably you get very anxious and say I have to get to take care of this like yesterday and the answer is for most young woman with cancer is that we have that time, that we can actually be able to save some eggs for her for after her cancer is cured and again, we have known this for guys for years, we have been able to take sperm from young men and freeze them and save them, but now we can get eggs from young women and we have that time and opportunity to do so.

Hochster That is excellent news, so even if we takes an extra week or two, it is worth it.

Minkin Absolutely, as I said it is not going to harm the cancer prognosis and we can let these young ladies become moms later on. Hochster It is all very exciting. Ratner It is. It is new paradigm, you know, things are changing, this is not the old days, we are not just taking care of cancers, we are taking care of them smartly, we are coming up with treatments that will not just take care of the cancer, but also will allow women to have quality of life and that is again something that we really want to do. We want to be able for the women to be able to live their lives.

Dr. Elana Ratner is an Associate Professor of Obstetric, Gynecology, and Reproductive Sciences and Dr. Mary Jane Minkin is a Clinical Professor of Obstetric, Gynecology, and Reproductive Sciences at Yale School of Medicine. If you have questions, the address is canceranswers@yale.edu and past editions of the pro-

gram are available in audio and written form at YaleCancerCenter.org. I am Bruce Barber reminding you to tune in each week to learn more about the fight against cancer. You are on WNPR, Connecticut's public media source for news and ideas